L Number	Hits	Search Text	DB	Time stamp
1	820	800/$2.ccls.	USPAT; US-PGPUB; JPO; JPO; DERWENT	2002/05/29 16:52
7	1	800/$2.ccls. and scurfy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/29 16:53
13	16	scurfy or fkhsf	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/29 16:56
25	1	Brunkow-mary$3.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/29 16:57
31	0	Ramsdell-fred.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/29 16:58
37	18852	transgenic	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/29 16:58
43	13	transgenic SAME (scurfy or sf or FKHsf)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/29 16:59
49	2	(US-20020016974-$).did. or (WO-200009693-$).did.	US-PGPUB; DERWENT	2002/05/29 17:00

(FILE 'HOME' ENTERED AT 16:30:27 ON 29 MAY 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 16:31:05 ON 29 MAY 2002

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L1        217872 S TRANSGEN?
L2           374 S L1 AND (SCURFY OR SF OR FKHSF)
L3           163 DUP REM L2 (211 DUPLICATES REMOVED)
L4           163 FOCUS L3 1-
L5            81 S L3 AND PY<=1998
L6            81 SORT L5 PY
L7             3 S L6 AND (SCURFY (L) TRANSGENIC)
L8            76 S L6 AND TRANSGENIC
L9            20 S SCURFY (L) TRANSGENIC
L10            7 DUP REM L9 (13 DUPLICATES REMOVED)
L11            7 SORT L10 PY
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=> d an ti so au ab pi l11 1-7

L11 ANSWER 1 OF 7 MEDLINE
AN 95015867 MEDLINE
TI CD4+CD8- T cells are the effector cells in disease pathogenesis in the scurfy (sf) mouse.
SO JOURNAL OF IMMUNOLOGY, (1994 Oct 15) 153 (8) 3764-74.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
AU Blair P J; Bultman S J; Haas J C; Rouse B T; Wilkinson J E; Godfrey V L
AB Mice hemizygous for the X-linked mutation, **scurfy** (sf), exhibit a fatal lymphoreticular disease that is mediated by T lymphocytes. To evaluate the respective roles of CD4 or CD8 single positive T cells in **scurfy** disease, neonates were treated with mAbs directed against the CD4 or CD8 molecules. Whereas mice treated with an anti-CD8 Ab developed lesions and succumbed to disease at the same time (17 days) as their untreated **scurfy** littermates, mice treated with an anti-CD4 Ab lived up to 11 wk before developing **scurfy** disease. To insure a more complete elimination of the T cell subsets, the **scurfy** mutation was bred onto beta 2-microglobulin (beta 2m)-deficient (CD8-less) and CD4-deficient **transgenic** mouse lines. Whereas there was little moderation of disease in beta 2m-deficient **scurfy** mice, CD4-deficient **scurfy** mice had markedly decreased **scurfy** lesions and a prolonged life span, similar to that of anti-CD4-treated sf/Y mice. Additionally, **scurfy** disease was transplanted into H-2-compatible nude mice through the adoptive transfer of CD4+CD8- T cells, but not CD4-CD8+ T cells. Flow-cytometric analysis revealed that sf/Y mice have an increased percentage of activated CD4+ T cells in their lymph nodes. In addition, there is an increase in the in vitro production of cytokines in the cultured splenocytes of CD8-less, but not CD4-less, **scurfy** mice. These data suggest that CD4+ T cells are critical mediators of disease in the **scurfy** mouse.

L11 ANSWER 2 OF 7 AGRICOLA
AN 94:67361 AGRICOLA
TI Handbook of mouse mutations with skin and hair abnormalities : animal models and biomedical tools.
SO c1994 544 p. : ill. ; 27 cm
Publisher: Boca Raton : CRC Press, c1994.
Series: CRC series in dermatology
ISBN: 0849383722 (acid-free paper).
AU Sundberg, John P.

L11 ANSWER 3 OF 7 MEDLINE
AN 96152740 MEDLINE
TI Disease in the scurfy (sf) mouse is associated with overexpression of cytokine genes.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 161-5.
Journal code: EN5; 1273201. ISSN: 0014-2980.
AU Kanangat S; Blair P; Reddy R; Deheshia M; Godfrey V; Rouse B T; Wilkinson E
AB The murine X-linked lymphoproliferative disease **scurfy** is similar to the Wiskott-Aldrich syndrome in humans. Disease in

scurfy (sf) mice is mediated by CD4+ T cells. Based on similarities in **scurfy** mice and **transgenic** mice that overexpress specific cytokine genes, we evaluated the expression of cytokines in the lesions of sf mice by Northern blotting, quantitative reverse-transcription polymerase chain reaction (RT-PCR) and by hybridization in situ. Overall, the phenotypic characteristics of **scurfy** disease correlated well with increased interleukin (IL)-4 (lymphadenopathy), IL-6 (B cell proliferation, hypergammaglobulinemia), IL-7 (dermal inflammatory cell infiltration), and high levels of tumor necrosis factor-alpha (wasting).

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 2000:133832 CAPLUS
DN 132:190512
TI Gene causing the mouse scurfy phenotype and its human ortholog
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
IN Brunkow, Mary E.; Jeffery, Eric W.; Hjerrild, Kathryn A.; Ramsdell, Fred
AB The present invention relates generally to the discovery of novel genes which, when mutated, results in a profound lymphoproliferative disorder. In particular, a mutant mouse designated Scurfy was used to identify the gene responsible for this disorder through backcross anal., phys. mapping, and large-scale sequencing. Isolated nucleic acid mols. are provided which encode Fkhsf, as well as mutant forms, which belongs to a family of related genes, all contg. a winged-helix DNA binding domain. The mouse Fkhsf gene spans .apprx.14 kb and contains 11 coding exons; the cDNA spans a coding region of 1287 bp and encodes a protein of 429 amino acids. The human ortholog to mouse Fkhsf cDNA is also provided. Also provided are expression vectors suitable for expressing such nucleic acid mols., and host cells contg. such expression vectors. Utilizing assays based upon the nucleic acid sequences disclosed herein (as well as mutant forms thereof), numerous mols. may be identified which modulate the immune system.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000009693	A2	20000224	WO 1999-US18407	19990811
WO 2000009693	A3	20000615		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9955594	A1	20000306	AU 1999-55594	19990811
EP 1105479	A2	20010613	EP 1999-942154	19990811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L11 ANSWER 5 OF 7 MEDLINE
AN 2001164244 MEDLINE
TI The murine mutation scurfy (sf) results in an antigen-dependent lymphoproliferative disease with altered T cell sensitivity.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (2001 Jan) 31 (1) 196-204.
Journal code: EN5; 1273201. ISSN: 0014-2980.
AU Zahorsky-Reeves J L; Wilkinson J E
AB The **scurfy** (sf) murine mutation results in a rapidly fatal lymphoproliferative disease, causing death by 26 days. Mature CD4+ T cells which tested hyperresponsive to T cell receptor (TCR) stimulation are involved. When sf was bred onto a **transgenic** line (DO11.10) in which 75 - 95 % of the T cells express TCR for ovalbumin (OVA) 323 - 339, sf / Y OVA mice had prolonged lifespans and less severe clinical symptoms compared to controls. However, sf / Y OVA mice eventually developed disease and died with manifestations similar to those of the original sf strain. The Rag1 knockout (KO) mouse, which cannot produce mature T (or B) cells without the addition of functional transgenes, was chosen for further breeding. The combination of Rag1 KO, the OVA transgene, and sf produced mice with 100 % of their mature DO11.10 alpha beta T cells

reactive strictly to OVA peptide. None of these Rag1 - / - sf / Y OVA mice developed the **scurfy** disease. They retained central deletion capability in vivo, but demonstrated an altered in vitro response to OVA peptide. These results indicate that mice without TCR for endogenous antigens do not develop **scurfy** symptoms, and are consistent with the hypothesis that the sf mutation requires antigen stimulation to manifest disease, perhaps via altered TCR sensitivity.

L11 ANSWER 6 OF 7 MEDLINE
AN 2002168091 MEDLINE
TI A **transgenic** mouse strain with antigen-specific T cells (RAG1KO/sf/OVA) demonstrates that the **scurfy** (sf) mutation causes a defect in T-cell tolerization.
SO COMPARATIVE MEDICINE, (2002 Feb) 52 (1) 58-62.
Journal code: 100900466.
AU Zahorsky-Reeves Joanne L; Wilkinson J Erby
AB The scurfy (sf) murine mutation causes severe lymphoproliferation, which results in death of hemizygous males (sf/Y) by 22 to 26 days of age. The CD4+ T cells are crucial mediators of this disease. Recent publications have not only identified this mutation as the genetic equivalent of the human disease X-linked neonatal diabetes mellitus, enteropathy, and endocrinopathy syndrome, but also have indicated that the defective protein-scurfin-is a new forkhead/winged-helix protein with a frameshift mutation, resulting in a product without the functional forkhead. These results have lead to speculation that the scurfy gene acts by disrupting the T-cell tolerance mechanism, resulting in hyperresponsiveness and lack of down-regulation. The Rag1KO/sf/Y OVA strain, with virtually 100% of its CD4+ T cells reactive strictly to ovalbumin (OVA) peptide 323-339, is an excellent model for determination of the sf mutation's ability to disrupt tolerance. We hypothesized that Rag1KO/sf/OVA mice would not be tolerant to antigen at a dose that tolerizes control animals. We found that splenic cells from Rag1KO/sf/Y OVA mice injected with the same dose of OVA peptide that induces tolerance in cells from control mice proliferate in vitro in response to OVA peptide. These results are consistent with a defect in the pathway responsible for peripheral T-cell tolerization.

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 2002:209700 CAPLUS
DN 136:324025
TI A **transgenic** mouse strain with antigen-specific T cells (RAG1KO/sf/OVA) demonstrates that the **scurfy** (sf) mutation causes a defect in T-cell tolerization
SO Comparative Medicine (2002), 52(1), 58-62
CODEN: COMEFT
AU Zahorsky-Reeves, Joanne L.; Wilkinson, J. Erby
AB The scurfy (sf) murine mutation causes severe lymphoproliferation, which results in death of hemizygous males (sf/Y) by 22 to 26 days of age. The CD4+ T cells are crucial mediators of this disease. Recent publications have not only identified this mutation as the genetic equiv. of the human disease X-linked neonatal diabetes mellitus, enteropathy, and endocrinopathy syndrome, but also have indicated that the defective protein, scurfin, is a new forkhead/winged-helix protein with a frameshift mutation, resulting in a product without the functional forkhead. These results have lead to speculation that the scurfy gene acts by disrupting the T-cell tolerance mechanism, resulting in hyperresponsiveness and lack of down-regulation. The Rag1KO/sf/Y OVA strain, with virtually 100% of its CD4+ T cells reactive strictly to ovalbumin (OVA) peptide 323-339, is an excellent model for detn. of the sf mutation's ability to disrupt tolerance. The authors hypothesized that Rag1KO/sf/OVA mice would not be tolerant to antigen at a dose that tolerizes control animals. The authors found that splenic cells from Rag1KO/sf/Y OVA mice injected with the same dose of OVA peptide that induces tolerance in cells from control mice proliferate in vitro in response to OVA peptide. These results are consistent with a defect in the pathway responsible for peripheral T-cell tolerization.

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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF' ENTERED AT 16:31:05 ON 29 MAY 2002

L1 217872 S TRANSGEN?
L2 374 S L1 AND (SCURFY OR SF OR FKHSF)
L3 163 DUP REM L2 (211 DUPLICATES REMOVED)
L4 163 FOCUS L3 1-
L5 81 S L3 AND PY<=1998
L6 81 SORT L5 PY
L7 3 S L6 AND (SCURFY (L) TRANSGENIC)
L8 76 S L6 AND TRANSGENIC

=> d an ti so au ab pi l8 21 27 60 64

L8 ANSWER 21 OF 76 MEDLINE
AN 96152740 MEDLINE
TI Disease in the **scurfy** (**sf**) mouse is associated with overexpression of cytokine genes.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1996 Jan)** 26 (1) 161-5.
Journal code: EN5; 1273201. ISSN: 0014-2980.
AU Kanangat S; Blair P; Reddy R; Deheshia M; Godfrey V; Rouse B T; Wilkinson E
AB The murine X-linked lymphoproliferative disease **scurfy** is similar to the Wiskott-Aldrich syndrome in humans. Disease in **scurfy** (**sf**) mice is mediated by CD4+ T cells. Based on similarities in **scurfy** mice and **transgenic** mice that overexpress specific cytokine genes, we evaluated the expression of cytokines in the lesions of **sf** mice by Northern blotting, quantitative reverse-transcription polymerase chain reaction (RT-PCR) and by hybridization in situ. Overall, the phenotypic characteristics of **scurfy** disease correlated well with increased interleukin (IL)-4 (lymphadenopathy), IL-6 (B cell proliferation, hypergammaglobulinemia), IL-7 (dermal inflammatory cell infiltration), and high levels of tumor necrosis factor-alpha (wasting).

L8 ANSWER 27 OF 76 MEDLINE
AN 95015867 MEDLINE
TI CD4+CD8- T cells are the effector cells in disease pathogenesis in the **scurfy** (**sf**) mouse.
SO JOURNAL OF IMMUNOLOGY, **(1994 Oct 15)** 153 (8) 3764-74.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
AU Blair P J; Bultman S J; Haas J C; Rouse B T; Wilkinson J E; Godfrey V L
AB Mice hemizygous for the X-linked mutation, **scurfy** (**sf**), exhibit a fatal lymphoreticular disease that is mediated by T lymphocytes. To evaluate the respective roles of CD4 or CD8 single positive T cells in **scurfy** disease, neonates were treated with mAbs directed against the CD4 or CD8 molecules. Whereas mice treated with an anti-CD8 Ab developed lesions and succumbed to disease at the same time (17 days) as their untreated **scurfy** littermates, mice treated with an anti-CD4 Ab lived up to 11 wk before developing **scurfy** disease. To insure a more complete elimination of the T cell subsets, the **scurfy** mutation was bred onto beta 2-microglobulin (beta 2m)-deficient (CD8-less) and CD4-deficient **transgenic** mouse lines. Whereas there was little moderation of disease in beta 2m-deficient **scurfy** mice, CD4-deficient **scurfy** mice had markedly decreased **scurfy** lesions and a prolonged life span, similar to that of anti-CD4-treated **sf**/Y mice. Additionally, **scurfy** disease was transplanted into H-2-compatible nude mice through the adoptive transfer of CD4+CD8- T cells, but not CD4-CD8+ T cells. Flow-cytometric analysis revealed that **sf**/Y mice have an increased percentage of activated CD4+ T cells in their lymph nodes. In addition, there is an increase in the in vitro production of cytokines in the cultured splenocytes of CD8-less, but not CD4-less, **scurfy** mice. These data suggest that CD4+ T cells are critical mediators of disease in the **scurfy** mouse.

L8 ANSWER 60 OF 76 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 94:498096 SCISEARCH
TI TRANSPLANTATION OF T-CELL-MEDIATED, LYMPHORETICULAR DISEASE FROM THE

SCURFY (**SF**) MOUSE

SO AMERICAN JOURNAL OF PATHOLOGY, (**AUG 1994**) Vol. 145, No. 2, pp. 281-286.
ISSN: 0002-9440.

AU GODFREY V L (Reprint); ROUSE B T; WILKINSON J E

AB The X-linked mutation, **scurfy** (**sf**), causes a fatal lymphoreticular disease characterized by runting, lymphadenopathy, splenomegaly, hypergammaglobulinemia, exfoliative dermatitis, Coombs'-positive anemia, and death by 24 days of age. T lymphocytes are required to mediate this syndrome as shown by a total absence of disease in mice bred to be **scurfy** and nude (**sf**/Y; nu/nu). The **scurfy** phenotype is not transmitted by **sf**/Y bone marrow transplants, though cells of **scurfy** origin do reconstitute all lymphoid organs in the recipient mouse. These data suggest that **scurfy** disease results from an abnormal T cell development process and not from an intrinsic stem cell defect. We therefore tested the ability of transplanted **scurfy** thymuses to transmit **scurfy** disease to congenic euthymic mice, to athymic (nude) mice, and to severe combined immunodeficiency (SCID) mice. Euthymic recipients of **sf**/Y thymic grafts remained clinically normal as did all SCID and nude recipients of normal thymus transplants. Morphological lesions similar to those found in **scurfy** mice occurred in all H-2-compatible nude and SCID recipients of **sf**/Y thymic grafts. Intraperitoneal injections of **scurfy** thymocytes, splenocytes, and lymph node cells also transmitted the **scurfy** phenotype to H-2-compatible nude mice and SCID mice. Our findings indicate that **scurfy**, disease cas be transmitted to T cell-deficient mice by engraftment of **scurfy** T cells, but that pathogenic **scurfy** T cell activities can be inhibited (or prevented)) ill immunocompetent recipient mice.

L8 ANSWER 64 OF 76 CAPLUS COPYRIGHT 2002 ACS

AN 1997:564325 CAPLUS

DN 127:174597

TI Analysis of pathological changes of liver and digestive tract in HGF/**SF transgenic** mice

SO Front. Gastroenterol. (**1997**), 2(3), 252-260
CODEN: FRGAF7; ISSN: 1342-1484

AU Takayama, Hisashi; Sakata, Hiromi; Shimoda, Ryuya; Nagamine, Takeaki; Takagi, Hitoshi

AB A review, with 35 refs., on prepn. of **transgenic** mice expressing human hepatocyte growth factor (HGF)/scatter factor (**SF**), and abnormal development, enhancement of liver regeneration, and hepatoma formation in the HGF/**SF transgenic** mice. Usefulness of the HGF/**SF transgenic** mice as animal model for the studies of morphogenesis, regeneration, and neoplastic transformation in the liver and digestive tract is discussed.

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L3 163 DUP REM L2 (211 DUPLICATES REMOVED)
L4 163 FOCUS L3 1-
L5 81 S L3 AND PY<=1998
L6 81 SORT L5 PY
L7 3 S L6 AND (SCURFY (L) TRANSGENIC)

=> d an ti so au ab l7 1-3

L7 ANSWER 1 OF 3 MEDLINE
AN 96152740 MEDLINE
TI Disease in the **scurfy** (**sf**) mouse is associated with overexpression of cytokine genes.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1996 Jan)** 26 (1) 161-5.
Journal code: EN5; 1273201. ISSN: 0014-2980.
AU Kanangat S; Blair P; Reddy R; Deheshia M; Godfrey V; Rouse B T; Wilkinson E
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L7 ANSWER 2 OF 3 MEDLINE
AN 95015867 MEDLINE
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Journal code: IFB; 2985117R. ISSN: 0022-1767.
AU Blair P J; Bultman S J; Haas J C; Rouse B T; Wilkinson J E; Godfrey V L
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L7 ANSWER 3 OF 3 AGRICOLA
AN 94:67361 AGRICOLA
TI Handbook of mouse mutations with skin and hair abnormalities : animal models and biomedical tools.

SO **c1994** 544 p. : ill. ; 27 cm
Publisher: Boca Raton : CRC Press, c1994.
Series: CRC series in dermatology
ISBN: 0849383722 (acid-free paper).
AU Sundberg, John P.

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